REMARKS

Claims 37-57 are pending. Claims 37-57 have been rejected on various grounds.

In this response, applicants amend claims 37, 39, 43, 47, 48, 52, 53, 54, and 57. Reconsideration and allowance are requested in view of the amendments and below arguments.

Applicants thank the Examiner for entering the amendment filed on October 26, 2000; withdrawal of objections of claims 37, 43, 48, 51; withdrawal of 35 USC 101 rejections of claims 54-56; withdrawal of 35 USC 112, second paragraph rejections of claims 54-56; and withdrawal of 35 USC 112, first paragraph rejections of claims 53-56.

Sequence Requirement

Applicants amend claim 54 per Examiner's suggestion. Reconsideration and allowance are requested.

Specification

Applicants have amended specification the following Examiner's suggestion (also per paper # 11 and 13, section 2a).

Applicants have amended specification following the Examiner's suggestion (also per paper # 11 and 13, section 2b). Applicant add an "abstract" of the disclosure as published under WO 97/31944, which does not constitute "a new matter".

Claim Objections

The Examiner objected to claims 39, 47, and 48 because of informalities. Applicants amend claims per Examiner's suggestion and as appropriate. Reconsideration and allowance are solicited.

Double Patenting Objections

The Examiner has rejected the claims 37, 51 and 57 for double patenting over claims 2 and 10 of US Patent No. 5,833,989. The Examiner further asserts that "the claims of instant application use the open language of "having"[] the patent claims read on the claims of the instant application and render the instant claims obvious". Applicants points out that the claims of the instant application implicate an SCR3-derive polypeptide containing only 6 to 23 amino acids, or multimers thereof. Applicants amend the claims 37, 51 and 57 further narrating the specific size of the polypeptide fragment of SCR3. Reconsideration and allowance are solicited.

Enablement Rejections

On pages 3-4 the Examiner rejected claims 37-57, for reasons set forth in previous office actions paper # 11 section 5a. Examiner asserts that the "claims are not limited to polypeptides 23 amino acids or fewer". In response the Applicants amend the claims and the amended claims for "polypeptide containing at least 6 and no more than 23 amino acid residues", or multimers thereof are supported by the specification of the instant application. Reconsideration and allowance of claims 37-57 are solicited.

The Examiner has also rejected the claims 37-57 and asserts that the data on anti-complement activity (Example 5 on activity of E1 SEQ ID NO:4) "does not provide support for function of the great breadth of polypeptides encompassed by the claims". In response, the Applicants point out that there is adequate experimental support and data for the claimed polypeptides are shown in examples (e.g., Example 5 on anti-complement activities of the polypeptides) of originally filed application. Applicants further point out that in the specification as filed, the anti-complement activity of the peptides was demonstrated using a hemolytic assay which is a standard assay method known in the art for measuring anti-complement activity. Experimental data indicate that all polypeptides, having sequence GGRKV and/or FELVGEPSIY, as described in the application and as defined in amended claims are active in the hemolytic assay. Therefore, withdrawal of the rejection is solicited.

Definiteness Rejections

The Examiner rejects claims 37-57 and on page 5, which refers to paper # 13, section 4, which again refers back to paper # 11 sections 6a through 6j of the Office Actions on indefiniteness grounds.

For definiteness, a claim need only reasonably apprise those skilled in the art of the utilization and scope of the invention. *Hybritech, Inc. v. Monoclonal Antibodies,* 231 USPQ 81, 94-95 (1986). Words are to be given their plain meaning as understood by the person of ordinary skill in the art, particularly given the limitations of the English language. *See* MPEP §§ 707.07(g); 2111.01 (Rev. 1, February 2000). Claims are to be given their broadest reasonable interpretation consistent with applicants' specification. *See* MPEP § 2111 (Rev. 1, February 2000). In sum, in order to reject the claims on definiteness grounds, it is incumbent on the examiner to show how and why the skilled person having applicants' specification would not be apprised of the invention by the language-at-issue. The rejections are discussed below.

6a~6j) The Examiner rejected claims for using various terms or phrases for example, 'SRC3-derived', 'portion of sequence', 'having', 'at least one of the carboxy terminus', 'lysine derivative', 'altered at specific position to remove chemically reactive amino acids', 'SCR repeat', 'inserted in a region', and 'SCR3'. In response, Applicants amend claims as appropriate and as suggested by the Examiner.

However, Applicants also respectfully disagree with the Examiner on various terms and phrases used and point out that SCR (or SRC as noted in the Office Actions, which we believe are meant for SCR by the Examiner) the abbreviated "Short Consensus Repeats" or a species SCR3 is well known in the art, particularly given related patents from Mossakowska *et al.* (See, for example, US Patent No. 5,833,989). The term 'derivative' or the 'SCR-derivative' is also well known in the art and the Applicants point out that the "derivatives" are the polypeptides comprising SCRs, well known in the art (See, for example, US Patent No. 5,833,989 and 5,859,223).

Applicants further point out that the amended claims are clear and understandable with respect to the phrase 'portion of sequence' within the SEQ ID NO: 1 while the claims most

definitely describes the portions (a) GGRKVF (6-11 OF SEQ ID NO: 1), and (b) FELVGEPSIY (residues 11-20 of SEQ ID NO: 1).

Again the Applicants point out that the term 'SCR repeat' is not unclear as there are only 30 short consensus repeats (SCR) in CR1 and this was well known in the art at the time the application was filed (See, for example, page 691, paragraph 1, lines 2-4 and page 693, right column, last paragraph, in Birmingham *et al.* J. Immunol. 153(2):691-700)(1994)) (enclosed).

Per the Examiner's suggestion, the first independent claim is amended and the full name of the region as SCR3 is recited. Therefore, withdrawal of the rejections is solicited.

Anticipation Rejection

On page 5 of the final Office Action, the Examiner rejected the claims 37, 39, and 51-57 and alleges as being anticipated by Fearon *et al.* for reasons recorded by the Examiner in previous Office Actions paper #s 13 and 11. The Examiner asserts that "the claims are not limited to a specific size polypeptide" and "Fearon discloses human CR1. SCR3 is a portion thereof []. Therefore the sequence is disclosed by Fearon". In response the Applicants amend the claims and point out that the claims read a specific size polypeptide of SCR3.

However, Applicants respectfully disagree with the Examiner and further point out that the disclosure in Fearon *et al.* does not anticipate any small fragment of SCR3 of the current invention and there is no data or teaching in Fearon suggesting which of the 69 amino acids of SCR3 might comprise the active portion of the CR1 fragment. The instant application discloses for the first time that there is an active fragment of CR1 which resides within the SCR3 portion of the molecule. The activity of the invented fragment has further been demonstrated to be due to the portions (a) GGRKVF (6-11 OF SEQ ID NO: 1), and (b) FELVGEPSIY (residues 11-20 of SEQ ID NO: 1). Furthermore the original specification of the instant application supports the claims and recorded data showing that fragments containing these sequences are active (see Example 5 in the specification). Therefore, withdrawal of the rejections is solicited.

Obviousness Rejections

On page 5 of the Final Office Action, the Examiner has rejected claims 48-50 as obvious over Fearon *et al.* in combination with Capon *et al.* The Examiner alleges that "Fearon does not have deficiencies with respect to what is claimed". In response the Applicants respectfully traverse the rejection and refer the arguments of the above paragraph made in order to obviate the alleged §102 rejection. In view of the above argument, the Applicants point out that Capon *et al.* does not rectify the deficiencies in Fearon *et al.*

At the outset, Applicants note the examiner must show all of the recited claim elements in the combination of references that make up the rejection. When combining references to make out a *prima facie* case of obviousness, the examiner is obliged to show by citation to specific evidence in the cited references that (i) there was a suggestion to make the combination and (ii) there was a reasonable expectation that the combination would succeed. Both the suggestion and reasonable expectation must be found within the prior art, and not be gleaned from applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); *see also* MPEP §§ 2142-43 (Rev. 1, February 2000).

When an examiner alleges a *prima facie* case of obviousness, such an allegation can be overcome by showing that (i) there are elements not contained in the references or within the general skill in the art, (ii) the combination is improper (for example, there is a teaching away or no reasonable expectation of success) and/or (iii) objective indicia of patentability exist (for example, unexpected results). *See U.S. v. Adams*, 383 U.S. 39, 51-52 (1966); *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d 1923, 1927 (Fed. Cir. 1990); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 230 USPQ 416, 419-20 (Fed. Cir. 1986).

Applicants further point out that Fearon *et al.* discloses the CR1 sequence but does not teach which of the many SCRs that make up the CR1 protein is active, or that activity could be found in a portion of one specific SCR. Furthermore, Capon *et al.* discloses large plasma protein and not a small discrete peptide and therefore does not provide any motivation to combine Fearon and Capon. Moreover, at the time of filing of the instant application, skilled artisan would not consider combining large CR1 (protein) fragments with another large protein

until there was an indication as to what the active CR1 fragment is and how large it is, which was not provided until the current invention. Moreover, even if someone had tried, the resulting chimeric protein would not be any of what is claimed in the instant application, but rather would be a large plasma protein in combination with a large fragment of CR1, which is contrary to the present invention.

Thus, at the time the invention was made, there would have been no "reasonable expectation of success," to produce polypeptides of current invention, even while having the knowledge of Fearon *et al.* and in combination with the disclosure of Capon *et al.*

Applicants therefore submit that the Examiner has not established a *prima facie* case of obviousness, and therefore respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing remarks and amendments, reconsideration of the application and allowance of the claims are requested. If any issues remain which the Examiner believes could be resolved through a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at 202-912-2777.

Respectfully submitted,

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MARKED UP AMENDED CLAIMS

37. **A[n] short consensus repeat-3 (SCR3)**-derived polypeptide **[having 6 to 23] containing at least 6 and no more than 23** amino acid residues and comprising **[at least]** a portion of Sequence (I) (SEQ ID NO: 1): CNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSG (I), wherein the polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) GGRKVF (6-11 OF SEQ ID NO: 1), and

(b) FELVGEPSIY (residues 11-20 of SEQ ID NO: 1).

39. The SCR3- derived polypeptide according to claim 37, further comprising a chemically reactive amino acid residue **[at least one of] located at one or both of a position selected from the group consisting of** the carboxyl terminus and the amino terminus of the polypeptide.

43. A multimeric polypeptide comprising at least two SCR3-derived polypeptides **[having 6 to 23] containing at least 6 and no more than 23** amino acid residues and comprising **[at least]** a portion of Sequence (I) (SEQ ID NO: 1): CNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSG (I), wherein the polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) GGRKVF (residues 6-11 of SEQ ID NO: 1), and

(b) FELVGEPSIY (residues of 11-20 of SEQ ID NO: 1), wherein the polypeptides are linked to a core structure.

47. The multimeric polypeptide according to claim 43, which comprises $(lys)_4$ $(lys)_2$ Ala-OH[)] (SEQ ID NO: 6) linked through N-(ε-thiopropionyl) linkers that are disulfide bonded to cysteine thiol of the **[poly peptide] <u>polypeptide</u>** SGGRKVFELVGEPSIYC (SEQ ID NO: 5).

48. A chimeric polypeptide comprising a host protein and an SCR3-derived polypeptide **[having 6 to 23] <u>containing at least 6 and no more than 23</u>** amino acid residues and comprising **[at least]** a portion of Sequence (I) (SEQ ID NO: 1): CNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSG (I), wherein the polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) GGRKVF (residues 6-11 of SEQ ID NO: 1), and

(b) FELVGEPSIY (residues 11-20 of SEQ ID NO: 1), wherein the SCR3-derived polypeptide is inserted in a region of the host protein that is not essential to the overall architecture or folding pathway of **[a] <u>said</u>** host protein.

52. A process for preparing an SCR3-derived polypeptide **[having 6 to 23] <u>containing at least 6 and no more than 23</u>** amino acid residues and comprising **[at least]** a portion of Sequence (I) (SEQ ID NO: 1): CNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSG (I), wherein the polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) GGRKVF (residues 6-11 of SEQ ID NO: 1), and

(b) FELVGEPSIY (RESIDUES 11-20 of SEQ ID NO: 1), comprising the step of: condensing peptide units.

53. A process for preparing an SCR3-derived polypeptide **[having 6 to 23]** **containing at least 6 and no more than 23** amino acid residues and comprising **[at least]** a portion of Sequence (I) (SEQ ID NO: 1): CNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSG (I), wherein the polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) GGRKVF (residues 6-11 of SEQ ID NO: 1), and

(b) FELVGEPSIY (residues 11-20 of SEQ ID NO: 1), comprising the step of: expressing DNA encoding the SCR3-derived polypeptide in a recominant host cell, and recovering the SCR3-derived polypeptide.

54. An isolated polynucleotide encoding an SCR3-derived polypeptide **[having 6 to 23]** **containing at least 6 and no more than 23** amino acid residues, wherein the SCR3-derived polypeptide comprises **[at least]** a portion of Sequence (I) (SEQ ID NO: 1): CNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSG (I), wherein the SCR3-derived polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) GGRKVF (residues 6-11 of SEQ ID NO: 1), and

(b) FELVGESPIY (residues 11-20 of SEQ ID NO: 1).

57. A pharmaceutical composition comprising

(1) a therapeutically effective amount of an SCR3-derived polypeptide **[having 6 to 23]** **containing at least 6 and no more than 23** amino acid residues and comprising **[at least]** a portion of Sequence (I) (SEQ ID NO: 1): CNPGSGGRKVFELVGEPSIYCTSNDDQVGIWSG (I), wherein the polypeptide has at least one amino acid sequence selected from the group consisting of:

(a) GGRKVF (residues 6-11 of SEQ ID NO: 1), and

(b) FELVGEPSIY (residues 11-20 of SEQ ID NO: 1), and

(2) a pharmaceutically acceptable carrier or excipient.

chimeric protein would not be any of what is claimed in the instant application, but rather would be a large plasma protein in combination with a large fragment of CR1, which is contrary to the present invention.

Thus, at the time the invention was made, there would have been no "reasonable expectation of success," to produce polypeptides of current invention, even while having the knowledge of Fearon *et al.* and in combination with the disclosure of Capon *et al.*

Applicants therefore submit that the Examiner has not established a *prima facie* case of obviousness, and therefore respectfully request withdrawal of the rejection.

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Respectfully submitted,

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